can be used. A significant advantage of the present invention is that the preferred microorganisms, especially when grow

In under aerobic conditions, can utilize minimal media. The anaerobic production typically will not require additional nutrients, so the final product can be isolated from a relatively clean fermentation broth using any of a variety of separation techniques. Liquid-liquid extraction is a well-known technique for the separation of organic acids from fermentation broths, and results in considerable purification. With the present invention it is believed that simpler, less costly, less energy-consuming systems may also be useful.

In one embodiment, the present invention uses genetically modified yeast having a crabtree-negative phenotype in a train-type process that induces a "switch" in the metabolic pathway after a critical cell density has been reached and at which time it is desired to dramatically increase the specific productivity of the desired organic product. A typical method for inducing the metabolic pathway switch is by moving the biomass from a highly aerated vessel to a substantially anaerobic vessel, causing oxygen starvation. It is noted that a common carbohydrate (*e.g.*, glucose or xylose) can be used as the carbon source during both the growth phase and the production phase. The use of a genetically modified yeast cell having a crabtree-negative phenotype can be critical to the success of this embodiment. In addition, the specific productivity of the desired organic product can be critical to success. The term "specific productivity" as used herein reflects the amount of product produced and is represented as the number of grams of organic product produced per gram of biomass (dry weight) per hour, i.e., g/(g * hour). Typically, the specific productivity for organic products such as lactate and acrylate is greater than about 0.1 g/(g * hour), for example, greater than about 0.2 g/(g * hour), or greater than about *0.5* g/(g * hour). By providing a high specific productivity as described herein, the energy required for cell maintenance may be obtained via the fermentative product pathway under substantially anaerobic conditions, rather than relying on aeration to generate high amounts of energy via the respiratory pathway.

It is noted that substantially anaerobic vessels are aerated at a rate of less than about 0.1 VVM. Under certain production situations, no aeration will be used. In

addition, the yield (*i.e.*, g organic product/g carbon source consumed) in this embodiment typically is greater than about 70 wt%, and is produced without the addition of carbon sources such as ethanol and acetate. In some cases, in order to achieve the specific productivity required to generate the required energy for cell maintenance, it may be necessary to enhance the pathway from glucose to pyruvate in addition to providing the necessary enzymes to produce the desired product.

In another embodiment, the train-type process can be designed such that only the highly aerated growth vessel is equipped with sterilization capability. The anaerobic production vessel is typically operated at temperatures greater than about 35°C (e.g., greater than about 36, 37, 38, 39, 40, 41, 42, 43, 44, or 45°C). Few wild-type yeast will be able to survive and compete with the genetically modified yeast at such temperatures as the pH drops during product production, especially since they will not have an enhanced fermentation pathway that can generate energy for cell maintenance, in addition, the yeast can be engineered to contain "killer plasmids" as described herein, which can prevent yeast from other species from surviving. The invention also provides various methods for culturing yeast cells. For example, a yeast cell having a crabtree-negative phenotype can be cultured with culture medium either having an organic ph value less than about 3.0, or containing a corn fiber hydrolysate. Other methods for culturing yeast cells include, without limitation, culturing yeast cells having a crabtree-negative phenotype at a temperature greater than about 35°C with culture medium either having an inorganic pH value less than about 3.0, or containing a pentose carbon or corn fiber hydrolysate.

Further, the invention provides a process for making an organic product. This process includes growing a microorganism under culture conditions, and changing the culture conditions to promote production of the organic product. In this process, the microorganism has reduced pyruvate decarboxylase, alcohol dehydrogenase, aldehyde dehydrogenase, and/or acetyl-CoA synthase activity, and exhibits a growth rate in the absence of ethanol and acetate that is at least about 30 percent (*e.g.*, about 35, 40, 50, 75, 100, 150, 200 percent, or more) of that observed in a corresponding microorganism not having reduced pyruvate decarboxylase, alcohol dehydrogenase, aldehyde dehydrogenase, and/or acetyl-CoA synthase activity. Typically, culture